Influenza and Pneumococcal Vaccines in Asthmatic Patients: Benefits and Risks

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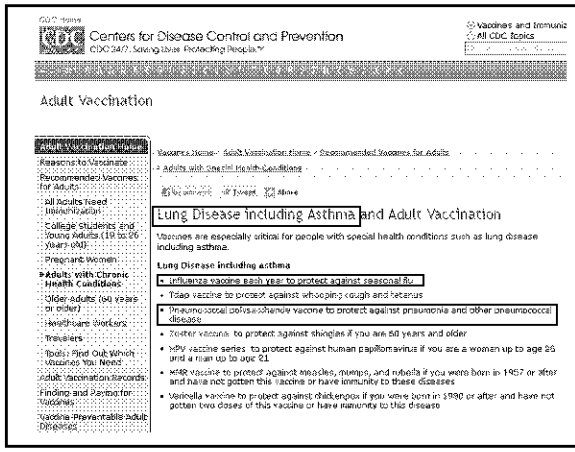
Faculty Disclosure Information

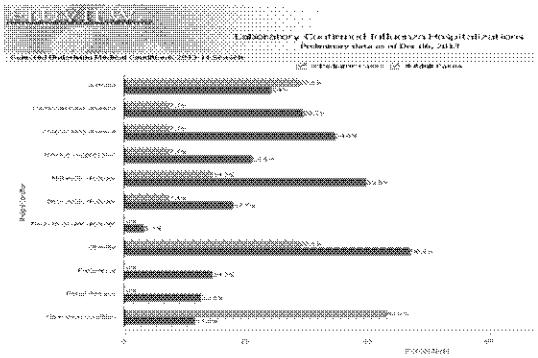
- I have not had a financial interest or other relationship with the manufacturers of the products that will be discussed in my presentation.
- This presentation will not include discussion of pharmaceuticals or devices that have not been approved by the FDA.
- I will not be discussing unapproved or "off-label" uses of pharmaceuticals or devices.

Objectives

- Review current influenza and pneumococcal vaccine recommendations for patients with asthma including the rationale for these recommendations



Asthma is a major risk factor for influenza hospitalization



http://gis.cdc.gov/grasp/fluview/FluHospChars.html

Increased H1N1 infection rate in asthma

SUBJECTS

- 161 children aged 4-12 years followed through influenza season:
  - –95 with asthma
  - –66 without asthma
- Provided 8 weekly nasal mucus samples analyzed for respiratory viruses
- URI and asthma symptoms, morning PEFR and albuterol use recorded

Kloepfer KM, et al J Respir Crit Care Med 2012;185:1275-9.

Increased H1N1 infection rate in asthma

RESULTS

- 34% of children infected with H1N1
  - with asthma (41%)
  - without asthma (24%)
  - OR, 2.2; 95% CI, 1.1–4.4; P = 0.03
- Rates of loss of asthma control:
  - H1N1 38%
  - rhinovirus, 21%
  - combination rhinovirus and H1N1, 44%

Kloepfer KM, et al J Respir Crit Care Med 2012;185:1275-9.

CDC

- **Recent studies show vaccine can reduce the risk of flu illness by about 60% among the overall population during seasons when most circulating flu viruses are like the viruses the flu vaccine is designed to protect against.**

http://www.cdc.gov/flu/about/qa/vaccineeffect.htm

Does IIV cause asthma exacerbations?

TABLE 2. FREQUENCY OF EXACERBATIONS OF ASTHMA WITHIN 3 AND 14 DAYS AFTER VACCINE AND PLACEBO INJECTIONS.

EVENT	NO. OF PATIENTS IN ANALYSIS*	VACCINE INJECTION	PLACEBO INJECTION	ABSOLUTE DIFFERENCE (95% CI)†
		percent		
New or increased use of oral corticosteroids				
Within 3 days after injection	1952	2.0	2.0	0.1 (−0.8 to 0.9)
Within 14 days after injection	1952	5.3	5.1	0.2 (−1.2 to 1.6)
Unscheduled use of health care for asthma symptoms				
Within 3 days after injection	1952	1.3	1.8	−0.5 (−1.3 to 0.3)
Within 14 days after injection	1952	5.5	5.1	0.4 (−1.0 to 1.8)
Increased use of rescue medication				
Within 3 days after injection	1858	6.1	6.5	−0.4 (−1.9 to 1.1)
Within 14 days after injection	1858	15.2	14.8	0.7 (−1.5 to 2.8)
≥20% decrease in peak expiratory flow rate from personal best‡				
Within 3 days after injection	1861	7.5	8.2	−0.8 (−2.8 to 0.8)
Within 14 days after injection	1865	16.7	16.6	0.1 (−1.8 to 2.0)
Any of the above§				
Within 3 days after injection	1952	12.7	13.8	−1.1 (−3.0 to 0.9)
Within 14 days after injection	1952	28.8	27.7	1.1 (−1.4 to 3.6)

ALA. N Engl J Med 2001;345:1529-36.)

Does LAIV cause asthma exacerbations?

- Some studies have shown a small increased rate of wheezing episodes after receipt of LAIV, particularly in children under age 3 years
- This risk has not been consistently shown across studies or across influenza seasons in the same study
- Most studies administering LAIV to children age 2 years and older with asthma have not shown exacerbations

CDC

- ACIP recommends *against* use in the following:
  - children aged 2 through 4 years whose parents or caregivers report that a health-care provider has told them during the preceding 12 months that their child had wheezing or asthma or whose medical record indicates a wheezing episode has occurred during the preceding 12 months
  - persons with asthma

Morbidity & Mortality Weekly Report 2013;62:RR-7

Influenza vaccination of egg-allergic patients

- Patients who have IgE-mediated egg allergy have a theoretical risk of anaphylaxis if injected with influenza vaccines containing egg protein.
- Withholding influenza vaccine from egg-allergic recipients has very real risk, namely the morbidity and mortality associated with the disease.

Influenza vaccine contains measurable quantities of egg protein (ovalbumin); does this cause systemic reactions when injected into egg-allergic patients?

- 28 published studies involving >4300 egg-allergic subjects getting influenza vaccine without *any* serious reactions (no respiratory distress or hypotension), and with only a low rate of minor reactions (hives, mild wheezing).
- So, the answer appears to be no.

But what about patients with severe egg allergy?

- Most studies have specifically *included* patients with histories of severe anaphylaxis (n = 656) with egg ingestion and these patients also tolerate the vaccine.
- So, even these patients do not appear to be at risk of serious reaction.

Why are there no serious reactions being reported?

- manufacturers of injectable trivalent influenza vaccine (IIV) report the maximum amount of ovalbumin < 1 mcg per 0.5 mL dose.
- The measured amounts in independent laboratories are usually much lower than the claimed amounts.

What about LAIV?

- Although the intranasally-administered live attenuated influenza vaccine (LAIV) contains a low amount of ovalbumin, all published studies to date have evaluated the injectable inactivated influenza vaccine (IIV), and thus IIV rather than LAIV should be used for egg-allergic recipients.
- Also LAIV should not be used in children with asthma, which often coexists with egg allergy.

What about non-egg-based IIV?

- Two non-egg-based influenza vaccines have recently been approved by the FDA for use in patients 18 years of age and older.
- They should not be used in patients under age 18 because some influenza vaccines have been found to be less immunogenic in certain age groups and others have been found to have higher rates of adverse reactions in certain age groups, and the risk of the egg-based vaccines in egg-allergic patients is minimal.

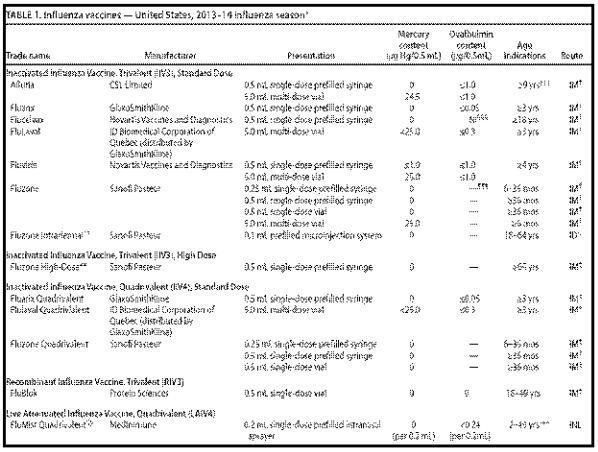
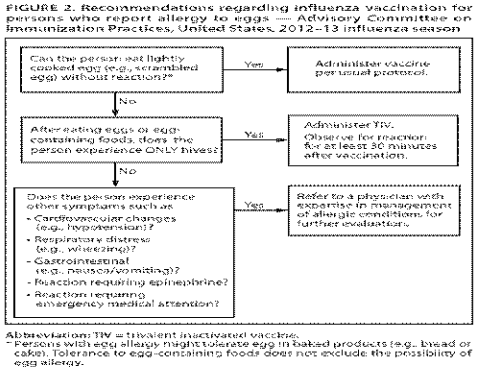


TABLE 1. Influenza vaccines — United States, 2013–14 influenza season*

Trade name	Manufacturer	Presentation	Mercury content (µg Hg/0.5 mL)	Ovalbumin content (µg/0.5mL)	Age indications	Route
Inactivated Influenza Vaccine, Trivalent (IIV3), Standard Dose						
Afluria	CSL Limited	0.5 mL single-dose prefilled syringe	0	≤1.0	≥9 yrs††	IM†
		5.0 mL multi-dose vial	24.5	≤1.0		
Fluzone	GlaxoSmithKline	0.5 mL single-dose prefilled syringe	0	≤0.05	≥3 yrs	IM†
Flucelvax	Novartis Vaccines and Diagnostics	0.5 mL single-dose prefilled syringe	0	§§§	≥18 yrs	IM†
FluLaval	ID Biomedical Corporation of Québec (distributed by GlaxoSmithKline)	5.0 mL multi-dose vial	≤25.0	≤0.3	≥3 yrs	IM†
Fluvirin	Novartis Vaccines and Diagnostics	0.5 mL single-dose prefilled syringe	≤1.0	≤1.0	≥4 yrs	IM†
		5.0 mL multi-dose vial	25.0	≤1.0		
Fluzone	Sanofi Pasteur	0.25 mL single-dose prefilled syringe	0	—¶¶	6–35 mos	IM†
		0.5 mL single-dose prefilled syringe	0	—	≥36 mos	IM†
		0.5 mL single-dose vial	0	—	≥36 mos	IM†
		5.0 mL multi-dose vial	25.0	—	≥6 mos	IM†
Fluzone Intradermal***	Sanofi Pasteur	0.1 mL prefilled microinjection system	0	—	18–64 yrs	ID***
Inactivated Influenza Vaccine, Trivalent (IIV3), High Dose						
Fluzone High-Dose†††	Sanofi Pasteur	0.5 mL single-dose prefilled syringe	0	—	≥65 yrs	IM†
Inactivated Influenza Vaccine, Quadrivalent (IIV4), Standard Dose						
Fluarix Quadrivalent	GlaxoSmithKline	0.5 mL single-dose prefilled syringe	0	≤0.05	≥3 yrs	IM†
FluLaval Quadrivalent	ID Biomedical Corporation of Québec (distributed by GlaxoSmithKline)	5.0 mL multi-dose vial	≤25.0	≤0.3	≥3 yrs	IM†
Fluzone Quadrivalent	Sanofi Pasteur	0.25 mL single-dose prefilled syringe	0	—	6–35 mos	IM†
		0.5 mL single-dose prefilled syringe	0	—	≥36 mos	IM†
		0.5 mL single-dose vial	0	—	≥36 mos	IM†
Recombinant Influenza Vaccine, Trivalent (RIV3)						
FluBlok	Protein Sciences	0.5 mL single-dose vial	0	0	18–49 yrs	IM†
Live Attenuated Influenza Vaccine, Quadrivalent (LAIV4)						
FluMist Quadrivalent§§§	MedImmune	0.2 mL single-dose prefilled intranasal sprayer	0 (per 0.2 mL)	<0.24 (per 0.2mL)	2–49 yrs¶¶¶	INL



"Other measures, such as dividing and administering the vaccine by a two-step approach and skin testing with vaccine, are not necessary"

Guillain-Barré´ syndrome

- "Swine flu" vaccine administered in 1976 associated with increased risk GBS (1 additional case per 100,000 over background rate of 1 to 2 cases per 100,000)
- Subsequent years influenza vaccines have shown no consistent increased risk (If any, 1 per million)
- Specific attention was paid to the potential for GBS after the 2009 pandemic influenza A (H1N1) vaccine campaign and no increased rate was found.

- GBS continues to be reported in temporal association with influenza infection itself
- Previous GBS has risk of a recurrence
- Persons who developed GBS within 6 weeks of influenza vaccination should avoid subsequent immunization
- However, individuals with a history of GBS unrelated to influenza infection or vaccination who would benefit from immunization can be vaccinated

Asthma increases the risk of invasive pneumococcal disease

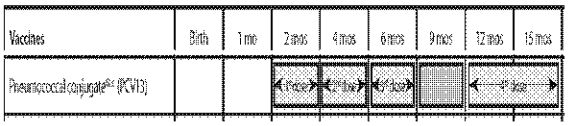
Table 2. Association between the Presence of Asthma and the Risk of Invasive Pneumococcal Disease

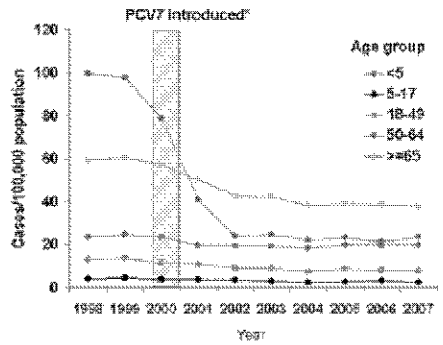
Variable	Case Subjects (N=635)	Controls (N=6350)	Adjusted Odds Ratio for Invasive Pneumococcal Disease (95% CI)*
	no./total no. (%)		
Any asthma	114/635 (18.0)	516/6350 (8.1)	2.4 (1.9–3.1)
High-risk asthma†	95/635 (15.0)	383/6350 (6.0)	2.6 (2.0–3.5)
Low-risk asthma	19/635 (3.0)	133/6350 (2.1)	1.7 (0.99–3.0)
Coexisting conditions that confer a high risk of invasive pneumococcal disease‡			
Absent	51/367 (14.7)	410/5542 (7.4)	2.4 (1.7–3.4)
Present	63/288 (21.9)	106/808 (13.1)	2.3 (1.3–4.1)
Age§			
2–4 yr	26/122 (21.3)	116/1220 (9.5)	2.3 (1.4–4.0)
5–17 yr	11/62 (17.7)	34/620 (5.5)	4.0 (1.5–10.7)
18–49 yr	77/451 (17.1)	366/4510 (8.1)	2.4 (1.8–3.3)

* ≥ 1 hospitalization or ED visit or oral corticosteroids or ≥ 3 albuterol MDIs / yr.

Talbot TR, et al. N Engl J Med. 2005;352:2082-90.

PCV13

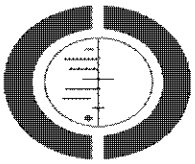




Pilishvili et al. JID 2010:201:32-41.

Vaccines for preventing pneumococcal infection in adults (Review)

Moberley S, Holden J, Tatham DP, Andrews RM



Moberley S, et al. Cochrane Database of Systematic Reviews 2013 Art. No.: CD000422

Cochrane

- 25 studies (18 RCTs involving 64,852 participants and seven non-RCTs involving 62,294 participants)
- Meta-analysis of the RCTs found strong evidence of pneumococcal polysaccharide vaccine (PPSV23) efficacy against invasive pneumococcal disease (OR 0.26, 95%CI 0.14 to 0.45.

Injection Site Reactions

Table 1: Incidence of Injection-Site and Systemic Complaints in Adults ≥50 Years of Age Receiving Their First (Initial) or Second (Revaccination) Dose of PNEUMOVAX 23 (Pneumococcal Polysaccharide Vaccine, 23 Valent) or Placebo Occurring at ≥1% in Any Group

	PNEUMOVAX 23 Initial Vaccination N=444	PNEUMOVAX 23 Revaccination* N=584	Placebo Injection† N=1008
Number Followed for Safety	438	549	984‡
	AE Rate	AE Rate	AE Rate
Injection-Site Complaints			
Solicited Events			
Pain/Soreness/Tenderness	60.0%	77.2%	7.7%
Swelling/Induration	20.3%	30.8%	2.8%
Erythema	16.4%	34.5%	3.3%

PNEUMOVAX 23. Package insert. Merck. Revised: 03/2013

Rare Reports of Anaphylaxis; 2 with positive skin tests

1. Ponvert C, Ardelean-Jaby D, Colin-Gorski AM, Soufflet B, Hamberger C, de Blic J, et al. Anaphylaxis to the 23-valent pneumococcal vaccine in child: a case-control study based on immediate responses in skin tests and specific IgE determination. Vaccine. 2001; 19:4588-91.
2. Wise RP, Iskander J, Pratt RD, Campbell S, Ball R, Pless RP, et al. Postlicensure Safety Surveillance for 7-Valent Pneumococcal Conjugate Vaccine. JAMA 2004; 292:1702-10.
3. Ponvert C, Scheinmann P, de Blic J. Anaphylaxis to the 23-valent pneumococcal vaccine: a second explored case by means of immediate-reading skin tests with pneumococcal vaccines. Vaccine 2010; 28:8256-7.

Summary

- Patients with asthma are more likely to get influenza and more likely to be hospitalized with influenza
- Influenza vaccine is approximately 60% effective at preventing influenza
- LAIV should not be given to (especially very young) children with asthma
- IIV can be safely administered to patients with egg allergy under observation

Summary

- Patients with asthma are more likely to get invasive pneumococcal disease
- Pneumococcal vaccine (PPSV23) is approximately 75% effective at preventing invasive pneumococcal disease and should be given to all adults 19 through 64 years of age with asthma (and all adults aged 65 and older)